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EFFECTS OF ALIROCUMAB, A FULLY HUMAN MONOCLONAL ANTIBODY TO PROPROTEIN CONVERTASE SUBTILISIN/KEXIN TYPE 9, ON LIPOPROTEIN PARTICLE CONCENTRATIONS DETERMINED BY NUCLEAR MAGNETIC RESONANCE: SUBSTUDY OF A RANDOMIZED DOUBLE-BLIND PHASE II CLINICAL TRIAL

Poster Contributions
Hall C
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Background: Alirocumab reduces low-density lipoprotein cholesterol (LDL-C) and apolipoprotein B (apo B), but its effect on LDL particle (LDL-P) and other lipid particle concentrations has not been determined. Standard LDL-C assays measure cholesterol content rather than particle numbers. Compared to LDL-C, LDL-P concentration may more closely estimate cardiovascular risk.

Methods: This substudy of a Phase II trial (NCT01288443) included patients with LDL-C ≥100mg/dL who received placebo (n=31) or alirocumab 150 mg administered subcutaneously (SC) every 2 weeks (Q2W) (n=26) on top of stable daily atorvastatin (10-40 mg). Nuclear magnetic resonance spectroscopy measured concentrations of total LDL-P, very low-density lipoprotein particles (VLDL-P), high-density lipoprotein particles (HDL-P) and lipoprotein subclasses in samples from before and after 12 wks of treatment.

Results: The table shows particle concentrations before and after alirocumab 150mg SC Q2W vs placebo. Alirocumab reduced mean LDL-P by 63% vs 1% for placebo (P<0.0001) and median VLDL-P by 36% vs a 33% increase for placebo (P<0.0001). HDL-P levels increased 11% for alirocumab vs 1% for placebo (P<0.05). Changes in all particle subclasses were directionally similar.

Conclusions: Alirocumab significantly reduced LDL-P and other lipoprotein particles when added to stable statin therapy with a magnitude of reduction similar to its previously reported effect on LDL-C and apo B.

Table. Lipoprotein particle concentrations (nmol/L) for placebo (n=31) and alirocumab 150mg Q2W (n=26). *P<0.05; †P<0.0001 vs. placebo

Mean (sd) or median (Q1:Q3)	Placebo			Alirocumab 150 mg Q2W			
	Baseline	Week 12	% change	Baseline	Week 12	% change	
LDL	Total LDL	1422.5 (321.3)	1383.8 (327.9)	-1.0%	1320 (304.0)	475.4 (167.3)†	-63.3%†
	Intermediate density lipoprotein	110 (51:166.5)	57 (24.5:144.5)		84.5 (33:115)	37 (12:66)*	
	Large LDL	546.6 (205.3)	431.8 (217.4)		532.2 (212.9)	152.4 (107.6)†	
	Small LDL	755.3 (304.9)	847.6 (375.1)		666.5 (333.8)	279.9 (191.0)†	
VLDL +chylomicron	Total VLDL +chylomicron	61.9 (47.8:95.6)	83.9 (45:102.2)	33.4%	71.5 (36.9:94.1)	42.0 (30.5:54.1)†	-36.4%†
	Large VLDL +chylomicron	3.5 (2.1:8.5)	4.3 (1.8:9.4)		3.6 (1.8:8.5)	3.1 (1.7:6.9)	
	Medium VLDL	19.3 (13.1:33.9)	33.1 (13.1:51.9)		18.3 (10.7:50)	14.4 (8.2:26.9)†	
	Small VLDL	35.3 (28.2:47.8)	37.3 (25.4:56.3)		35.7 (25:49.5)	21.4 (19.9:26.7)*	
HDL	Total HDL	32.9 (6.4)	33.2 (7.4)	1.4%	32.6 (6.3)	36.1 (6.5)*	11.2%*
	Large HDL	3.8 (2.0)	3.9 (2.2)		4.8 (3.1)	6.1 (3.5)*	
	Medium HDL	9.2 (5.9:14.4)	8 (5.4:10.2)		7.8 (5.6:10.7)	9.8 (6.6:11.3)	
	Small HDL	18.8 (5.3)	21.3 (5.8)		19.4 (4.1)	20.0 (5.7)*	